REMARKS

Claims 1-4 and 6-8 are pending in the application. Claims 1-3 are canceled herein without prejudice or disclaimer. Claims 4 and 7 are amended herein for clarity to more particularly define the invention. Support for these amendments can be found throughout the specification as set forth below. It is believed that no new matter is added by these amendments and their entry and consideration are respectfully requested. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

Claim Objections

Claim 7 is objected to because formula 4 has been partly obscured. Claim 7 as presented herein shows the entire formula 4. Accordingly, applicants submit that this objection is obviated and respectfully request its withdrawal.

Claim rejections under 35 U.S.C. §112, paragraph 1 (Written Description)

Claims 4 and 6 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. Specifically, the Action alleges that the term "resistant to sugar hydrolase" as recited in claim 4 constitutes new matter because the ordinary definition of resistant encompasses the definitions from anything not completely unresistant to completely resistant.

Claim 4 is amended herein to recite wherein the glycopeptide has about 12 times higher resistance to Peptide-N Glycosidase F (PNGase F) than a glycopeptide comprising an asparagine-linked oligosaccharide. Support for this amendment can be found in the specification, at least, for example, in Test Example 1 on pages 22-23.

Accordingly, applicants submit that the rejection of claims 4 and 6 under 35 U.S.C. §112, first paragraph, is overcome and respectfully request its withdrawal.

Claim rejections under 35 U.S.C. §112, paragraph 2, Indefiniteness

Claims 4 and 6-8 are rejected under 35 U.S.C. §112, paragraph 2, for allegedly being indefinite.

A. Specifically, the Office Action alleges that claims 4 and 6 are indefinite for omitting essential structural cooperative relationships of elements such as the site on the oligosaccharide at which the thiol group of a peptide binds.

As presented herein, claim 4 recites that the aminated complex-type oligosaccharide binds to a thiol group of a peptide by displacement of halogen X of NH-(CO)-CH_2X. In addition, as presented herein, claim 7 recites bonding an aminated complex-type oligosaccharide of the formula (1) ... to a thiol group of the resulting peptide by displacement of halogen X of –NH-(CO)-CH_2X. Support for these amendments are found throughout the specification, at least, for example, in Example 2 on pages 19-21.

B. The Office Action further alleges that the term "resistant to sugar hydrolase" as recited in claim 4 is a relative term, which renders the claim indefinite.

As discussed above, claim 4 is amended herein to no longer recite resistant to sugar hydrolase but rather to recite wherein the glycopeptide has about 12 times higher resistance to PNGase F than a glycopeptide comprising an asparagine-linked oligosaccharide.

Accordingly, as presented herein claim 4 and claims 6-8 are clarified. Therefore, applicants submit that the rejections of claims 4 and 6-8 under 35 U.S.C. §112, paragraph 2, are overcome and respectfully request their withdrawal.

Claim rejections under 35 U.S.C. §103(a)

A. Claim 4 stands rejected under 35 U.S.C. §103(a) over Rademacher et al. (U.S. Patent No. 5280113) in view of Wong et al. (Biochem. J. 300:843-850 (1994)). Specifically, the Office Action states that it is well known in the art that N-glycanase cleaves N-acetyl-glucosamine from an asparagine residue. The Office Action further asserts that the glycopeptides made obvious by Rademacher et al. in view of Wong et al. do not form a bond between the oligosaccharide and asparagine but rather form a bond between the oligosaccharide and thiol groups. On this basis,

the Office Action concludes that one of ordinary skill in the art would reasonably expect that the glycopeptides made obvious by Rademacher et al. in view of Wong et al. would inherently have resistance to this sugar hydrolase, as N-glycanase is known to recognize a different substrate.

As discussed above, claim 4 is amended to recite that the glycopeptide has about 12 times higher resistance to PNGase F than a glycopeptide comprising an asparagine-linked oligosaccharide. Rademacher et al. and Wong et al. fail to teach or suggest the strength of the resistance to the PNGase F of a glycopeptide having a bond between the oligosaccharide and the thiol group as taught by the present invention.

Therefore, even if one of ordinary skill in the art believed that the glycopeptides of the present invention inherently have resistance to sugar hydrolase, they could not have reasonably expected that the bond between the oligosaccharide and the thiol group would have 12 times higher resistance to PNGase F than a bond between the oligosaccharide and asparagine based on a reading of Rademacher et al. and Wong et al. as taught by the present invention.

Accordingly, applicants submit that claim 4 is patentable over the cited references and respectfully request the withdrawal of this rejection.

B. Claim 6 stands rejected under 35 U.S.C. §103(a) over Rademacher et al. in view of Wong et al. in further view of Wright et al. (*Trends Biotechnol.* 15:26-32 (1997)).

For the same reasons as set forth above, applicants submit that claim 6 is non-obvious over Rademacher et al. in view of Wong et al.

Further Wright et al. fails to remedy the deficiencies of Rademacher et al. and Wong et al. Wright et al. discusses antibodies and that they are glycosylated at conserved regions. However, Wright et al. fails to teach or suggest a glycopeptide having about 12 times higher resistance to PNGase F than a glycopeptide comprising an asparagine-linked oligosaccharide as taught by the presently claimed invention.

Accordingly, applicants submit that claim 6 is patentable over the cited references and respectfully request the withdrawal of this rejection.

C. Claim 7 stands rejected under 35 U.S.C. §103(a) over Rademacher et al. in view of

Wong et al. in further view of Lee et al. (U.S. Patent No. 5,807,943). Specifically, the Office Action concedes that Rademacher et al. in view of Wong et al. fail to disclose a process for preparing a glycopeptide as taught by the presently claimed invention. The Office Action states that Lee et al. teaches it is known in the art to synthesize neoglycoconjugates such as neoglycoprotiens by using an endo-N-acetylglucosamidinase that performs both sugar hydrolase and transglycosylation functions or a process that hydrolyzes the oligosaccharide and substitutes a new oligosaccharide at the same time. On this basis, the Office Action asserts that it would have been obvious to one of ordinary skill in the art to combine Rademacher et al. in view of Wong et al. and in further view of Lee et al. to prepare a glycopeptide by cleaving a saccharide of a glycopeptide by sugar hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide and bonding an aminated complex-type oligosaccharide derivative to the resulting peptide at the same time. Applicants respectfully disagree for at least the reasons set forth below.

Claim 7 is amended herein to recite a process for preparing a uniform glycopeptide composition comprising steps of (a) and (b) that are performed at the same time, (a) cleaving an asparagine-linked oligosaccharide of a glycopeptide from a peptide by Peptide-N Glycosidase F (PNGase F) , wherein the resulting peptide has a thiol group, and (b) bonding an aminated complex-type oligosaccharide of the formula (1) ... to a thiol group of the resulting peptide by displacement of halogen X of –NH-(CO)-CH_2X. Thus, the sugar hydrolase is defined as PNGase F and the oligosaccharide cleaved in step (a) is an asparagine-linked oligosaccharide. Support for these amendments is found in the specification at least, for example, on page 9, lines 20-24, in Test Example 1 (pages 22-23) and in Example 2 (pages 19-21). Furthermore, with regard to uniformity of the compositions, the glycopeptide composition was identified by NMR as shown in Example 2 of the specification (pages 19-21). All peaks were identified as originating from the desired glycopeptide shown on page 21 of the specification, and no other peaks originating from other compounds were detected. Thus, the NMR data shows that the compositions include only the desired glycopeptide without any by-product and thus the compositions produced by the methods of the present invention are uniform.

The Office Action points out that Lee et al. discloses endo-N-acetylglucosamidinase, an enzyme that performs both sugar hydrolase and transglycosylation functions. However, applicants note that endo-N-acetylglucosamidinase can only cleave between the GlcNAc-GlcNAc bond in the oligosaccharide and transfer an oligosaccharide to GlcNAc-Asn. In other words, the bond that endo-N-acetylglucosamidinase cleaves by its hydrolase activity is the same bond that is formed by its transferase activity. Thus, Lee et al. does not teach or suggest changing the oligosaccharides, each having a different bond between the peptide and itself, by using the difference in resistance to the enzyme between the bond cleaved and the bond formed as is taught by the present invention.

Further, the hydrolase activity of the endo-N-acetylglucosamidinase is stronger than its transferase activity (see, Lee et al. col. 1, line 52). Thus, when a glycopeptide is treated with the endo-N-acetylglucosamidinase enzyme in a one pot system as suggested in the Office Action, a mixture of more than two types of glycopeptides would be produced, i.e., hydrolyzed/not hydrolyzed glycopeptides and glycosyl-transferred/not glycosyl-transferred glycopeptides. Each type of glycopeptide would then achieve equilibrium in the one pot system. As a result, one of ordinary skill in the art would readily recognize that the process as proposed in the Office Action would produce a non-uniform mixture of oligosaccharides with non-uniform physiological activity.

In contrast, the present invention provides a method of producing glycopeptides that are uniform in both structure and physiological activity in a one pot system. The methods of the present invention are able to achieve this result in a one pot system at least because the bond cleaved by PNGase F in step (a) is different than the bond formed in step (b) and because the bond in step (b) has a much higher resistance to the PNGase hydrolase activity than the bond cleaved in step (a). Furthermore, in contrast to endo-N-acetylglucosamidinase, PNGase F has only hydrolase activity and because the bond formed between an oligosaccharide and a thiol group is highly resistant to cleavage by the PNGase F, the glycopeptides produced by the process of claim 7 are uniform in structure and have uniform physiological activity (see specification, page 9, lines 14-26, and Example 2, pages 19-21).

As discussed above, it had not been known prior to the present invention that the bond

between the oligosaccharide and the thiol group of the glycopeptides of the present invention has about 12 times higher resistance to PNGase F than a glycopeptide comprising an asparagine-linked oligosaccharide. The process of claim 7 was first accomplished as a result of the discovery by the present investigators of these characteristics of the bond between the oligosaccharide and the thiol group. It is the knowledge of the distinctive characteristics of the bond between the oligosaccharide and the thiol group in contrast with the characteristics known in the art about the bond between the oligosaccharide and the asparagine group and their different reactions to PNGase F that made the process for preparing glycopeptides as taught by the present invention successful. Without this knowledge, one of ordinary skill in the art could not have conceived of the present invention.

Accordingly, applicants respectfully submit that Rademacher et al., Wong et al. and/or Lee et al., alone or in combination, fail to teach or suggest each of the recitations of claim 7. Therefore, applicants submit that claim 7 is patentable over the cited references and respectfully request the withdrawal of this rejection.

D. Claim 8 stands rejected under 35 U.S.C. §103(a) over Rademacher et al. in view of Wong et al. in further view of Lee et al. and Wright et al.

For the same reasons set forth above, ppplicants submit that claim 8 is non-obvious over Rademacher et al. in view of Wong et al. in further view of Lee et al. Further, Wright et al. fails to remedy the deficiencies of Rademacher et al., Wong et al. and Lee et al.

Wright et al. discusses antibodies and that they are glycosylated at conserved regions. However, Wright et al. fails to teach or suggest a process for preparing a uniform glycopeptide composition comprising steps of (a) and (b) that are performed at the same time, (a) cleaving an asparagine-linked oligosaccharide of a glycopeptide from a peptide by Peptide-N Glycosidase F (PNGase F), wherein the resulting peptide has a thiol group, and (b) bonding an aminated complex-type oligosaccharide of the formula (1) ... to a thiol group of the resulting peptide by displacement of halogen X of –NH-(CO)-CH_2X as taught by the presently claimed invention.

Accordingly, applicants submit that claim 8 is patentable over the cited references and respectfully request the withdrawal of this rejection.

The points and concerns raised in the Action having been addressed in full herein, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested. Should there be any remaining concerns, the Examiner is encouraged to contact the undersigned attorney by telephone to expedite the prosecution of this application.

The Commissioner is authorized to charge Deposit Account No. 50-0220 in the amount of $130.00 for a one-month extension of time. This amount is believed to be correct. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on November 23, 2009.

Claire Wimberly